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Cell function

Protein groove aids membrane assembly

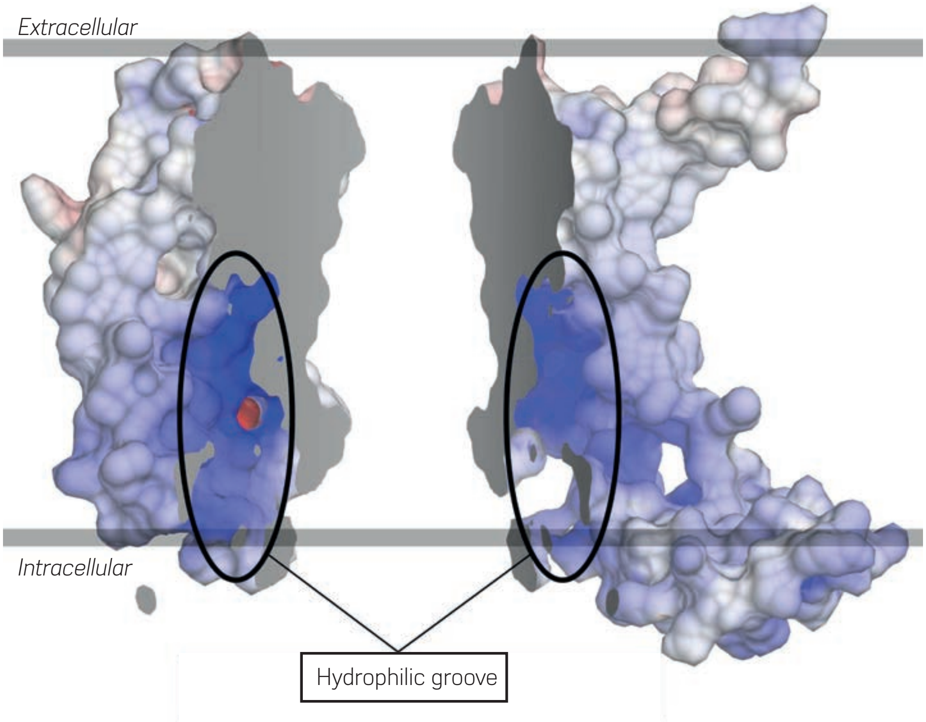
The crystal structure of a membrane protein in soil bacteria is described for the first time

Cell membranes are semi-permeable barriers, consisting of a bilayer of lipids with embedded proteins that perform vital functions. These proteins are so important that they have become the target of 60 per cent of the medicinal drugs used today.

For newly synthesized membrane proteins to properly function, they must be accurately inserted, folded and assembled into the membrane.

To help understand how this process occurs, Tomoya Tsukazaki and colleagues at NAIST described, for the first time, the crystal structure of YidC, a protein in the cytoplasmic membrane of *Bacillus halodurans*, a gram-positive bacterium found in soil[1]. "We determined the first high-resolution structure of the YidC–Oxa1–Alb3 family of membrane proteins, and we propose an insertion mechanism for membrane proteins," says Tsukazaki.

> **"Our findings pave the way for further investigations into the molecular mechanism of YidC."**



The membrane protein YidC's hydrophilic, positively charged groove facilitates membrane insertion of proteins.

YidC is involved in the folding and insertion of many membrane proteins, including one involved in the release of energy, and is thus essential for cell viability.

Tsukazaki's team collected diffraction data on YidC crystals at Japan's SPring-8 synchrotron facility, and refined the structure to a 2.4 ångström resolution. They then created computer simulations mimicking the physical movement of YidC in a lipid bilayer. To better understand YidC's role, they compared the effects of mutating the *yidC* gene to the effects of mutating another gene involved in the membrane insertion process.

Previous studies suggested YidC formed a channel that facilitated membrane insertion of protein substrates, says Tsukazaki. His team's investigations revealed, instead, that YidC contains a novel fold in which five independently functioning transmembrane helices form a groove that is open toward the lipid bilayer and cytoplasm, but closed on the extracellular side. The groove has an affinity for water (is hydrophilic) and positively charged (see figure).

A substrate protein interacts with the positively charged cytoplasmic region of YidC, and is then captured in YidC's hydrophilic groove; the positively charged groove attracting the negatively charged residue on the substrate. An arginine residue that exists in the groove participates in recognizing the substrate protein, which is then released by the groove into the membrane, partially facilitated by the membrane potential attracting the negatively charged residues on the substrate.

"Our findings pave the way for further investigations into the molecular mechanism of YidC," says Tsukazaki.

"YidC also facilitates the proper folding of membrane proteins inserted by a protein-conducting channel — the SecYEG translocon — and is essential for cell viability. We are trying to determine the structure of the complex of YidC and Sec proteins in order to fully understand the conserved mechanism of membrane protein biogenesis."

Reference

1. Kumazaki, K., Chiba, S., Takemoto, M., Furukawa, A., Nishiyama, K. *et al.* Structural basis of Sec-independent membrane protein insertion by YidC. *Nature* **509**, 516–520 (2014).

More information about the group's research can be found at the Membrane Molecular Biology Laboratory webpage: http://bsw3.naist.jp/eng/courses/courses309.html